PATENT
Attorney Docket No. **DOW-04647**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	G. Lomonossoff		
Serial No.:	09/580,704	Group No.:	1636
Filed:	05/30/2000	Examiner:	W. Sandals
Entitled:	**MODIFIED PLANT VIRUSES AS VECTORS**		

DECLARATION OF LADA RASOCHOVA, Ph.D., UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Dr. Lada Rasochova, under penalty of perjury, state that:

1. I am a scientist working in the field of expression of proteins in plants, including the expression of viral antigens in plant viral vectors. I am currently employed by the assignee, The Dow Chemical Co.

2. I have reviewed U.S. Patent Application Ser. No. 07/600,881.

3. I have reviewed the Office Action dated 08/29/2002, wherein the Examiner points to pages 12, 28, 24, 36, 39 and examples 17 and 28 in support of an argument that the '881 application describes "the insertion of a foreign peptide in the coat protein to produce a recombinant plant virus, such as cow pea mosaic virus" and more specifically "expressing a mammalian virus protein inserted into the plant virus coat protein" (page 5). It is respectfully submitted that the Examiner has misinterpreted the science taught in the '881 application.

4. Turning first to the experimental examples of the '881 application cited by the Examiner, Example 17 of the '881 application describes the manipulation of equine viral cDNA - *not plant viral genomic nucleic acid.* Moreover, Example 17 specifically notes that the vector containing the cDNA is digested with the appropriate restriction enzymes so as to

"delete the coding sequence of the coat protein." The text goes on to note that the deletion is confirmed by the inability of the resulting RNA to infect equine cells in culture. Thus, infectivity of plant cells is not discussed and there is no teaching of inserting a coding sequence for a foreign peptide into the coding sequence of plant viral coat protein.

5. While the Examiner does not discuss it, Example 20 of the 881 application describes the further manipulation of the nucleic acid of Example 17. Specifically, Example 17 teaches the insertion of the coding sequence of tyrosinase adjacent the promoter of the equine viral coat protein gene of Example 17. Again, plant viral genomic nucleic acid is not involved. Moreover, since the coding sequence for the equine viral coat protein gene is taught to be removed in Example 17, Example 20 says nothing about inserting a foreign gene into a coding sequence for a viral coat protein gene.

6. While the Examiner does not discuss it, Example 21 of the '881 application describes the further manipulation of the nucleic acid of Example 20. Specifically, Example 20 teaches that the host cell for the vectors of Example 20 is yeast - not plant cells. Examples 22 and 23 also do not deal with plant cells.

7. The Examiner specifically cites Example 28 of the '881 application. This example - like Example 17 - describes the manipulation of mammalian viral cDNA - *not plant viral genomic nucleic acid.* Example 29- like Example 17 - teaches the removal of the coding sequence for the coat protein. The text goes on to note that the deletion is confirmed by the inability of the resulting RNA to infect human cells in culture. Thus, infectivity of plant cells is not discussed and there is no teaching of inserting a coding sequence for a foreign peptide into the coding sequence of plant viral coat protein.

8. With respect to the pages of the '881 specification cited by the Examiner, it is respectfully submitted that the Examiner has misinterpreted these pages. Page 12 simply has a list of viruses - some of which infect mammalian cells and some of which infect plant cells - preceded by the sentence: " Some of the viruses which meet this requirement, and therefore are suitable, include . . .". Of course, to understand what "requirement" is being discussed on

Page 12 and what is "suitable," one must give it context by reading the preceding pages. For example, page 10 notes:

> "The present invention provides for the infection of a host, such as a prokaryotic or eukaryotic organism, cell or tissue, by a virus which has been modified so that the virus is transmissible but the viral nucleic acid is not infective."

Page 11 repeats this theme:

> "An important feature of the present invention is the preparation of nucleotide sequences which are capable of replication in a compatible host but which in themselves are incapable of infecting the host."

Page 11 goes to describe the first step of this process:

> "The first step in achieving any of the features of the invention is to modify the nucleotide sequences coding for the capsid protein . . ."

Then page 11 explains the list of viruses on page 12:

> "Therefore, any virus for which the capsid protein nucleotide sequence . . . have been identified *may be suitable* for use in the present invention . . ."

Thus, page 12 is merely listing those viruses for which the capsid protein nucleotide sequence has been identified - thereby making them "suitable."

9. Page 28 of the '881 specification also does not teach what the Examiner suggests. Page 28 merely teaches the use of OMV or RNV - or other plant viruses - to infect monocots. Looking on either side of page 28, one finds the theme (discussed in paragraph 8) repeated. For example, page 27 teaches that the coat protein coding sequences are altered or deleted. Thus, either the coding sequence has been completely deleted - or it has been altered - so as

to achieve the goal of ensuring that the first sequence "is not capable of transmission . . .". Thus, where the text speaks of inserting into the coding sequence of a coat protein, the coding sequence is NOT the native coding sequence - it is altered coding sequence.

10. Pages 34 and 36 of the '881 specification also do not teach what the Examiner suggests. Pages 34 and 36 merely teach the use of first and second vectors, the second vector encoding a viral coat protein for encapsidation. There is no teaching regarding inserting sequences into coding sequences for plant viral coat proteins.

11. Page 39 of the '881 specification also does not teach what the Examiner suggests. Page 39 merely lists the viruses with which agro-infection has been accomplished.

12. While the Examiner has not discussed it, Examples 1, 2 and 3 of the '881 specification teach the removal of the coding region for a plant virus coat protein and replacement with non-viral coding sequences. They do not teach the insertion of mammalian viral antigen coating sequences into the coding region for the coat protein of a plant virus.

Dated: 12-12-02

Lada Rasochova

Dr. Lada Rasochova